| | Туре | L# | Hits | Search Text | DBs | Time Stamp | Com Error ment Defini s tion ors | Error Error tion ors |
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| - | BRS | L1 | 116266 | 116266 promoter | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:35 | | 0 |
| 2 | BRS | L2 | 5516 | constitutive adj promoter | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:35 | | 0 |
| ω | BRS | L5 | 625 | molecular adj switch | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:56 | | 0 |
| 4 | BRS | L7 | 0 | 5 same 3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:36 | | 0 |
| 5 | BRS | 16 | 2 | 5 same 2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:36 | | 0 |
| 6 | BRS | L8 | 91 | (edwards adj cynthia.in.) or (fry adj kirk.in.) or (bruice adj thomas.in.) or (starr adj douglas.in.) or (laurance adj megan.in.) or (kwok adj | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:55 | <u>, </u> | 0 |
| 7 | BRS | L9 | 0 | 5 and 8 | USPÅT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:58 | | 0 |
| | BRS | L10 | 256 | gene adj switch | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:58 | | 0 |
| 9 | BRS | L11 | 0 | 10 and 8 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 12:58 | | 0 |
| 10 | BRS | L12 | 1873 | regulatable adj promoter | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:43 | | 0 |
| 11 | BRS | L13 | 2 | 5 same 12 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:42 | | 0 |
| 12 | BRS | L14 | 2 | 5527690.pn. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:43 | | 0 |
| 13 | BRS | L15 | 0 | 12 and 14 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:44 | | 0 |
| 14 | BRS | L16 | 13445 | inducible adj promoter | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:43 | | 0 |

| | Туре | L # | Hits | Search Text | DBs | d d | ment Defini s tion | ni Err ni ors |
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| 15 E | BRS | L17 | 1028 | 12 and 16 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:44 | | 0 |
| 16 E | BRS | L18 | 0 | 14 and 16 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:44 | | 0 |
| 17 E | BRS | L19 | 856 | 5 or 10 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 15:57 | | 0 |
| 18 B | BRS | L20 | 17692 | (transcription adj factor) or (transcriptional adj regulatory adj protein) or (transcriptional adj regulatory adj factor) or (DNA adj binding adj protein) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 | | 0 |
| 19 B | BRS | L21 | 3064 | (inducer or compound) same (DNA adj binding) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:00 | | 0 |
| 20 B | BRS | L22 | – | 19 same 20 same 21 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:41 | | 0 |
| 21 B | BRS | L23 | 14558 | dna adj binding | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:04 | · | 0 |
| 22 B | BRS | L24 | 661 | 20 same 21 same 23 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:09 | | 0 |
| 23 B | BRS | L25 | 14290 | 12 or 16 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:05 | | 0 |
| 24 B | BRS | L26 | 0 | 24 same 25 same transgene | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:06 | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | 0 |
| 25 B | BRS | L27 | 3688 | adenovirus adj vector | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:07 | | 0 |
| 26 B | BRS | L28 | 1381 | adeno-associated adj virus adj vector | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:07 | | 0 |
| 27 B | BRS | L30 | 0 | 29 same trangene | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:10 | | 0 |
| 28 B | BRS | L31 1 | 15255 | reporter adj gene | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/14 16:11 | | 0 |

*

| 29 | Type | L# | Hits 0 | Search Text 29 same 31 | g C | DBs USPAT; US-PGPUB; |
|----|------|-----|-----------|---|---------------------------------------|----------------------|
| 29 | BRS | L32 | 0 | 29 same 31 | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 30 | BRS | L29 | 18 | 20 same 19 same 23 | USPAT; US-PGPUB; EPO; JPO; DERWENT | GPUB; ERWENT |
| 31 | BRS | L33 | 0 | 29 same (12 or 16) | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 32 | BRS | L34 | 286 | DNA adj binding adj sequence | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 33 | BRS | L35 | 11443 | ul9 or NF-kappaB or gal4 or ZFHD1 orlacR or tetr lexa or (ecdysone adj receptor adj binding) | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 34 | BRS | L36 | 13319 | vp16 or nf-kappaB or gal4 or tfe3 or itf1 or oct-1 or sp1 or oct-2 or nfy-a or itf or cmyc or ctf | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 35 | BRS | L37 | 332178 | kruppel or krab or kox-1 or tetr or even-skipped or lacr or engrailed or hairy or hes or 332178 groucho or tle or ring1 or ssb16 or ssb24 or tup1 or nab1 or areb or e4bp4 or hoxa7 or ebna3 or mad or v-erba | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 36 | BRS | L38 | 2381 | (36 or 37) same 20 | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 37 | BRS | L39 | 0 | 35 same 38 same 19 | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |
| 38 | BRS | L40 | 70 | (repressor or activator) same 19 | USPAT; US-PGPUB; EPO; JPO; DERWENT | -PGPUB;)ERWENT |
| 39 | BRS | 141 | 29 | (repressor or activator) same 19 USPAT; US-PGPUB; same 20 EPO; JPO; DERWEN | USPAT; US-PGPUB; EPO; JPO; DERWENT | -PGPUB;)ERWENT |
| 40 | BRS | L42 | 0 | 41 same 21 | USPAT; US-PGPUB; EPO; JPO; DERWENT | PGPUB; ERWENT |

| l l | | | | | |
|------------------------------------|---------------------------------------|---------------------------------------|---------------------|---------------------------|-------------------------|
| | BRS | BRS | BRS | BRS | Туре |
| | L46 | L45 | L44 | L43 | L# |
| | | 101 | 0 | 2 | Hits |
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| 7 00 0000 | USPAT; US-PGPUB; EPO; JPO; DERWENT | USPAT; US-PGPUB; EPO; JPO; DERWENT | <u> </u> | Ţ | DBs |
| | 2003/09/14 16:41 | 2003/09/14 16:41 | 2003/09/14 16:40 | 2003/09/14 16:40 | Time Stamp |
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                                                     14 SEP 2003
 FILE 'CAPLUS' ENTERED AT 16:49:32 ON 14 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
 FILE 'BIOSIS' ENTERED AT 16:49:32 ON 14 SEP 2003
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FILE 'EMBASE' ENTERED AT 16:49:32 ON 14 SEP 2003 COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.
FILE 'SCISEARCH' ENTERED AT 16:49:32 ON 14 SEP 2003
COPYRIGHT 2003 THOMSON ISI
FILE 'AGRICOLA' ENTERED AT 16:49:32 ON 14 SEP 2003
=> s molecular switch
              4398 MOLECULAR SWITCH
=> s gene switch
12
               903 GENE SWITCH
=> s 11 or 12
              5291 L1 OR L2
=> s (transcription factor) or (transcriptional regulatory protein) or (transcriptional regulatory
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           417831 (TRANSCRIPTION FACTOR) OR (TRANSCRIPTIONAL REGULATORY PROTEIN)
                     OR (TRANSCRIPTIONAL REGULATORY FACTOR) OR (DNA BINDING PROTEIN)
=> s (inducer or compound)(p) (dna binding)
              7538 (INDUCER OR COMPOUND) (P) (DNA BINDING)
=> s 13 (p) 14 (p) 15
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ACCESSION NUMBER:
                            2002635673
                                                MEDLINE
DOCUMENT NUMBER:
                            22282001
                                           PubMed ID: 12395191
                            A Renilla luciferase-Aequorea GFP (ruc-gfp) fusion gene
TITLE:
                            construct permits real-time detection of promoter
                            activation by exogenously administered mifepristone in
                            vivo.
AUTHOR:
                            Yu Y A; Szalay A A
                           Division of Human Anatomy, Loma Linda University School of Medicine, Loma Linda, CA 92350, USA.

Mol Genet Genomics, (2002 Oct) 268 (2) 169-78.

Journal code: 101093320. ISSN: 1617-4615.

Germany: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)
CORPORATE SOURCE:
SOURCE:
PUB. COUNTRY:~
DOCUMENT TYPE:
LANGUAGE:
                            English
FILE SEGMENT:
                           Priority Journals 🐇
ENTRY MONTH:
                            200212
                           Entered STN: 20021024
Last Updated on STN: 20030105
ENTRY DATE:
                           Entered Medline: 20021213
       In this study, we used a steroid-induced promoter activation system as a ***molecular*** ***switch*** to study the exogenous activation of
AB
       transgene expression. This promoter activation system consists of three components: (1) a steroidal ***inducer*** drug, mifepristone (RU486)
      components: (1) a steroidal ***inducer*** drug, mifepristone (RU486), which binds to (2) a chimeric ***transcription*** ***factor***
       complex, consisting of the mutant human progesterone receptor fused to the yeast GAL4 ***DNA*** - ***binding*** domain and the activation
      domain of the herpes simplex virus protein VP16, and (3) a synthetic promoter, consisting of a series of GAL4 recognition sequences upstream of the adenovirus major late E1B TATA box, linked to a gene construct
```

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***transcription*** ***factor*** complex. Monitoring of induced gene expression was carried out using a low-light video camera and a UV microscope to detect luciferase and GFP, respectively. Using this activation system, we observed a 10- to 25-fold activation, depending on the ***inducer*** dose, of both luciferase and GFP expression in transiently transfected cells in comparison to cells that were not exposed to mifenristone. We further demonstrated activation of consequences.
        to mifepristone. We further demonstrated activation of gene expression
       from the promoter activation system in live animals. The plasmids PAP
       CMV-GL914VPc'SV, carrying the chimeric
                                                                    ***transcription***
       ***factor*** cassette, and plasmid p17x4-TATA-ruc-gfp, carrying the ruc-gfp reporter gene construct, were co-injected into limb muscles of nude mice. Following DNA injection, mifepristone (50 micro g/kg) was delivered by intraperitoneal injection. Thirty-six hours after DNA and mifepristone injection, significant Renilla luciferase activity was detectable in the limb muscles.
       detectable in the limb muscles. The promoter activation system was also
        demonstrated in limb muscles and livers of nude mice that had received
       transplants of ex vivo-modified cells, which were transiently transformed
       with both the chimeric activator plasmid and the ruc-gfp reporter plasmid
       prior to implantation. Significant Renilla activity and GFP fluorescence were detected externally in limb muscles and in the livers of anesthetized animals that had received an intraperitoneal injection of ***inducer***. This external monitoring method for observing inducible gene expression in live animals will facilitate experimental studies of fundamental
       questions of biological and therapeutic relevance. It will be especially
       valuable for the analysis of gene function at specific stages of animal
       development. The method should also be of general use in gene therapy,
       since it permits simultaneous monitoring of the expression levels of
       light-emitting proteins and therapeutic proteins originating from the activation of identical promoters.
       ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
                                     2000:628284 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                                     133:233573
TITLE:
                                     Inducible regulatory systems for control of gene
INVENTOR(S):
                                     Lim, Moon Young; Edwards, Cynthia A.; Fry, Kirk E.;
                                     Bruice, Thomas W.; Starr, Douglas B.; Laurance, Megan
                                     E.; Kwok, Yan
Genelabs Technologies, Inc., USA
PCT Int. Appl., 92 pp.
PATENT ASSIGNEE(S):
SOURCE:
                                     CODEN: PIXXD2
DOCUMENT TYPE:
                                     Patent
LANGUAGE:
                                     English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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                                         DATE
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                                                                                          DATE
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                                                                WO 2000-US5728
                                                                                          20000303
       wo 2000052179
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PRIORITY APPLN. INFO.:
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                                                                                         19990303
                                                           US 1999-154605P P
                                                                                          19990917
                                                           wo 2000-us5728
                                                                                    W
                                                                                         20000303
       Inducible gene_expression_systems regulated by a ligand are described.
       The system includes a nucleic acid construct which has a DNA response sequence for a ***transcriptional*** ***regulatory***
          ***protein***
                                                                                      ***compd***
```

operably linked to a promoter, a sequence in the vicinity of the DNA response sequence, a transgene under the control of the promoter; and a ***DNA*** ***binding***

Compd . In some cases. the ***mol*** ***switch*** ***compd*** . In some cases, the ***mol*** . ***switch further includes a nucleic acid sequence encoding a ***transcriptional*** ***regulatory*** ***protein*** ***switch*** system operably

AB

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linked to a second promoter. The invention further provides a method for screening ***compds*** for the ability to function in the ***mol**
                           system and thereby regulate gene expression.
=> d his
      (FILE 'HOME' ENTERED AT 16:49:01 ON 14 SEP 2003)
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             903 S GENE SWITCH
             5291 S L1 OR L2
          417831 S (TRANSCRIPTION FACTOR) OR (TRANSCRIPTIONAL REGULATORY PROTEIN
            7538 S (INDUCER OR COMPOUND)(P) (DNA BINDING)
                6 S L3 (P) L4 (P) L5
                2 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
=> s dna binding
         254485 DNA BINDING
=> s 13 (p) 14
            362 L3 (P) L4
=> s 19 (p) 18
            105 L9 (P) L8
=> s transgene or (reporter gene)
         163288 TRANSGENE OR (REPORTER GENE)
=> s 110 (p) 111
             17 L10 (P) L11
=> s promoter
         572487 PROMOTER
=> s 112 (p) 113
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=> s 115 not 17
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=> d 116 1 ibib abs
L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
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ACCESSION NUMBER:
DOCUMENT NUMBER:
                            135:148182
TITLE:
                            Molecular switches II system comprising
                            ligand-regulated DNA binding molecule and targeted DNA
                            binding site and its use in screening for desired
                            binding elements and gene regulation
INVENTOR(S):
                            Choo, Yen; Ullman, Christopher Graeme; Moore, Michael
                            Gendaq Limited, UK
PATENT ASSIGNEE(S):
SOURCE:
                            PCT Int. Appl., 193 pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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                        KIND DATE
                                                 APPLICATION NO.
                                                                    DATE
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                                                 WO 2001-GB187
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                         Α3
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L1 L2

L3

L8

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L10

L11

L12

L13

L16

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                                                    GB 2000-29901
                                                                              20001207
                                                                         Α
                                                    GB 1999-12635
                                                                              19990528
AB
            ***aene***
                               ***switch***
                                                  system comprising (i) a target nucleic
      acid mol.; (ii) a nucleic acid binding mol. which binds to the target
      nucleic acid mol. in a manner modulatable by a ligand; and (iii) the ligand is described. The ***DNA*** - ***binding*** ligand can
      modulate the interaction of the other two elements of the system which may
      both be derived from random libraries. The system is particularly
      intended for use to identify nucleic acid binding mols., targeted nucleic
      acid binding sites and modulating ligands, and to regulate transcription from one or more ***promoters*** in gene regulation. The selection of derivs. of the middle zinc finger of the ***transcription***
                                                        ***DNA***
                                                                           ***binding***
                            Zif268 with altered
      phage display library in the presence of small mols. including Distamycin
      A, or actinomycin D, or echinomycin is presented. The ***DNA***

***binding*** activity of these isolated phage clones are also modulated
      by ligands and their use in gene regulation are tested in vitro binding assay. The zinc finger ***DNA*** ***binding*** domain is also
                                                          ***binding***
                                                                               domain is also
      converted to the catalytic domain of FokI restriction enzyme for ligand
      modulation. The isolated zinc finger clones and HSV VP16 activation
      domain fusion protein is prepd. and the modulation of its transcriptional
      activity by ligands is demonstrated with a ***reporter*** ***gene** in vivo. Methods of isolating cognate target nucleic acids and screening for ligands, which affect the binding of a ***DNA*** ***binding***
      mol. to its cognate DNA target, are described by using 434 repressor of
      phage 434. The zinc finger protein/drug/DNA microarrays are also provided
      for the selection purpose.
=> d his
      (FILE 'HOME' ENTERED AT 16:49:01 ON 14 SEP 2003)
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      16:49:32 ON 14 SEP 2003
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L2
               903 S GENE SWITCH
L3
              5291 S L1 OR L2
L4
                       (TRANSCRIPTION FACTOR) OR (TRANSCRIPTIONAL REGULATORY PROTEIN
L5
                       (INDUCER OR COMPOUND)(P) (DNA BINDING)
L6
                  6 S L3 (P) L4 (P) L5
L7
                   DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8
           254485 S DNA BINDING
L9
               362 S L3 (P) L4
L10
               105 S L9 (P) L8
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L16
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=> s (regulatable or inducible) (w) promoter
L17
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L18
=> s nf-kappaB
L19
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L20
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          43442 L19 OR L20
L21
=> s vp16 or nf-kappab or gal4 or tfe3 or itf1 or oct-1 or sp1 or oct-2 or nfy-a or itf2 or cmyc o
L22
          83638 VP16 OR NF-KAPPAB OR GAL4 OR TFE3 OR ITF1 OR OCT-1 OR SP1 OR
                 OCT-2 OR NFY-A OR ITF2 OR CMYC OR CTF
=> s kruppel or krab or kox-1 or tetr or even-skipped or lacr or engrailed o hairy or hes or grouc
L23
          33096 KRUPPEL OR KRAB OR KOX-1 OR TETR OR EVEN-SKIPPED OR LACR OR
                 ENGRAILED O HAIRY OR HES OR GROUCHO OR TLE OR RING1 OR SSB16 OR
                 SSB24 OR TUP1 OR NAB1 OR AREB OR E4BP4 OR HOXA7 OR EBNA3 OR MAD
                 OR V-ERBA
=> s (122 or 123) (p) 14
L24
          35250 (L22 OR L23) (P) L4
=> s 121 (p) 18
           9870 L21 (P) L8
L25
=> s 13 (p) 124 (p) 125
              8 L3 (P) L24 (P) L25
=> duplicate remove 126
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L26
                4 DUPLICATE REMOVE L26 (4 DUPLICATES REMOVED)
=> s 127 not (17 or 116)
               3 L27 NOT (L7 OR L16)
=> d 128 1-3 ibib abs
L28 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:
                            2002:927602 CAPLUS
DOCUMENT NUMBER:
                            138:20483
TITLE:
                            An GHRH (somatoliberin) expression system inducible by
                            a ligand-specific Gene-Switch regulator protein and
                            therapeutic uses
INVENTOR(S):
                            Nordstrom, Jeffrey L.; Draghia-Akli, Ruxandra
PATENT ASSIGNEE(S):
                            Valentis, Inc., USA; Baylor College of Medicine
SOURCE:
                            PCT Int. Appl., 90 pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                                 APPLICATION NO.
                         KIND
                              DATE
                                                                    DATE
     wo 2002097099
                          Α1
                                20021205
                                                 WO 2001-US17573 20010530
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
              VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

The present invention provides for a regulated gene expression system for

20010529

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, PRIORITY APPLN. INFO.: US 2001-294316P P 2001

growth hormone releasing hormon ("GHRH") characterized by low basal expression and high specific flucibility. The inducible-expression system includes two expression cassettes. The first expression cassette includes a promoter driving the expression of a mol.-switch fusion protein which comprises a DNA binding domain, a transactivation domain and a ligand-binding domain. The fusion protein is characterized by an inability to auto-dimerize in the absence of an ligand-inducer. The second expression cassette includes the gene encoding GHRH controlled by an inducible promoter which is activated by the fusion protein dimerizing in the presence of the inducer and binding to the promoter. The present invention includes therapeutic methods for treating growth hormone-related deficiencies assocd. with the growth hormone pathway; growth hormone-related deficiencies assocd. with genetic disease; wasting symptoms assocd. with burn, trauma, cancer, AIDS, and bone loss, as in elderly, or post-fracture. By administering an exogenously supplied inducer the expression system can be activated and controlled. THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L28 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN 2002:927555 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 138:19945 Estrogen receptor ligand binding domain variants and TITLE: prepn. of novel ligands and use to construct mol. gene switches for pharmaceutical use Bracken, Kathryn Rene; De Los Angeles, Joseph E.; Huang, Ying; Kadan, Michael J.; Ksander, Gary M.; INVENTOR(S): Zerby, Dennis B. Novartis AG, Switz. SOURCE: PCT Int. Appl., 159 pp. CODEN: PIXXD2 Patent English

PATENT ASSIGNEE(S):

DOCUMENT TYPE: LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                       KIND
                             DATE
                                              APPLICATION NO.
                                                                DATE
     wo 2002097050
                        Α2
                              20021205
                                              WO 2002-US16946 20020531
     wo 2002097050
                        Α3
                              20030313
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,
                                                                         TT, TZ,
              UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
              TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 43559 A1 20030731 US 2002-157899 20020531
     US 2003143559
PRIORITY APPLN. INFO.:
                                          US 2001-294839P P
                                                                20010531
     Mutants of steroid receptor ligand binding domains and synthetic ligands
     which have specific binding affinities for these receptors are provided.
     The use of these LBD-ligand combinations for construction of selective
     "mol. gene switches" is disclosed. Methods of regulating gene function
     using these switches are provided as are pharmaceutical compns. contg. the novel ligands.
```

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ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS ON STN
                                1999:477732 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                                131:223928
                                Development of gene-switch transgenic mice that
TITLE:
                                inducibly express transforming growth factor .beta.1
                                in the epidermis
                                Wang, Xiao-Jing; Liefer, Kristin M.; Tsai, Sophia; O'Malley, Bert W.; Roop, Dennis R. Department of Cell Biology and Dermatology, Baylor College of Medicine, Houston, TX, 77030, USA
AUTHOR(S):
CORPORATE SOURCE:
SOURCE:
                                Proceedings of the National Academy of Sciences of the
                                United States of America (1999), 96(15), 8483-8488
                                CODEN: PNASA6; ISSN: 0027-8424
```

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal LANGUAGE: English

Previous attempts to establish transgenic mouse models to study the functions of transforming growth factor .beta.1 (TGF.beta.1) in the skin

revealed controversial roles for TGF.beta.1 in epidermal growth (inhibition vs. stimulation) are resulted in neonatal lethality To establish a viable transgenic model for studying functions of TGF beta.1 in the skin, we have now developed transgenic mice, which allow focal induction of the TGF.beta.1 transgene in the epidermis at different expression levels and at different developmental stages. This system, termed "gene-switch," consists of two transgenic lines. The mouse loricrin vector targets the GLVPC transactivator (a fusion mol. of the truncated progesterone receptor and the GAL4 DNA binding domain), and a thymidine kinase promoter drives the TGF.beta.1 target gene with GAL4 binding sites upstream of the promoter. These two transgenic lines were mated to generate bigenic mice, and TGF.beta.1 transgene expression was controlled by topical application of an antiprogestin. On epidermal-specific induction of the TGF.beta.1 transgene, the Brdurd labeling index in the transgenic epidermis decreased 6-fold compared with controls. Induction of the TGF.beta.1 transgene expression also caused epidermal resistance to phorbol 12-myristate 13-acetate-induced hyperplasia, with a redn. in both epidermal thickness and BrdUrd labeling compared with those in controls. In addn., TGF.beta.1 transgene expression induced an increase in angiogenesis in the dermis. Given that the TGF.beta.1 transgene can affect both the epidermis and dermis, this transgenic model will provide a useful tool for studying roles of TGF.beta.1 in wound-healing and skin carcinogenesis in the future. REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT => d his (FILE 'HOME' ENTERED AT 16:49:01 ON 14 SEP 2003) FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:49:32 ON 14 SEP 20034398 S MOLECULAR SWITCH 903 S GENE SWITCH 5291 S L1 OR L2 417831 S (TRANSCRIPTION FACTOR) OR (TRANSCRIPTIONAL REGULATORY PROTEIN 7538 S (INDUCER OR COMPOUND)(P) (DNA BINDING) 6 S L3 (P) L4 (P) L5 2 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED) 254485 S DNA BINDING 362 S L3 (P) L4 105 S L9 (P) L8

L1 L2 L3 L4 L5 L6 L7 **L8** L9 L10 L11 163288 S TRANSGENE OR (REPORTER GENE) L12 17 S L10 (P) L11 572487 S PROMOTER L13 L14 7 S L12 (P) L13 **L15** 3 DUPLICATE REMOVE L14 (4 DUPLICATES REMOVED) L16 S L15 NOT L7 **L17** 7266 s (REGULATABLE OR INDUCIBLE) (W) PROMOTER L18 0 S L12 (P) L17 L19 23346 S NF-KAPPAB L20 20191 S UL9 OR GAL4 OR ZFHD1 OR LACR OR TETR OR LOR (ECDYSONE RECEPTO L21 43442 S L19 OR L20 L22 83638 S VP16 OR NF-KAPPAB OR GAL4 OR TFE3 OR ITF1 OR OCT-1 OR SP1 OR L23 33096 S KRUPPEL OR KRAB OR KOX-1 OR TETR OR EVEN-SKIPPED OR LACR OR E 35250 S (L22 OR L23) (P) L4 9870 S L21 (P) L8 8 S L3 (P) L24 (P) L25 L26 L27 4 DUPLICATE REMOVE L26 (4 DUPLICATES REMOVED) 3 S L27 NOT (L7 OR L16) => s lim moon/au 2 LIM MOON/AU => s edwards cynthia/au L30 5 EDWARDS CYNTHIA/AU => s fry kirk/au L31 24 FRY KIRK/AU => s bruice thomas/au 9 BRUICE THOMAS/AU

=> s starr douglas/au

2 STARR DOUGLAS/AU

L33

```
L34
              0 LAURANCE MAGAN/AU
=> kwok yan/au
KWOK IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).
=> s kwok yan/au
L35
             26 KWOK YAN/AU
=> s 129 or 130 or 131 or 132 or 133 or 135
             68 L29 OR L30 OR L31 OR L32 OR L33 OR L35
L36
=> s 136 and 11
              1 L36 AND L1
L37
  s 137 not 17
L38
              0 L37 NOT L7
=> d his
     (FILE 'HOME' ENTERED AT 16:49:01 ON 14 SEP 2003)
     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     16:49:32 ON 14 SEP 2003
L1
            4398 S MOLECULAR SWITCH
L2
             903 S GENE SWITCH
L3
            5291 S L1 OR L2
L4
         417831 S (TRANSCRIPTION FACTOR) OR (TRANSCRIPTIONAL REGULATORY PROTEIN
L5
            7538 S (INDUCER OR COMPOUND)(P) (DNA BINDING)
L6
               6 S L3 (P) L4 (P) L5
L7
               2 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8
         254485 S DNA BINDING
L9
             362 S L3 (P) L4
L10
             105 S L9 (P) L8
L11
         163288 S TRANSGENE OR (REPORTER GENE)
L12
              17 S L10 (P) L11
         572487 S PROMOTER
113
                 S L12 (P) L13
                DUPLICATE REMOVE L14 (4 DUPLICATES REMOVED)
               1 S L15 NOT L7
           7266 S (REGULATABLE OR INDUCIBLE) (W) PROMOTER
               0 S L12 (P) L17
          23346 S NF-KAPPAB
          20191 S UL9 OR GAL4 OR ZFHD1 OR LACR OR TETR OR LOR (ECDYSONE RECEPTO
L20
          43442 S L19 OR L20
L21
          83638 S VP16 OR NF-KAPPAB OR GAL4 OR TFE3 OR ITF1 OR OCT-1 OR SP1 OR
L22
L23
          33096 S KRUPPEL OR KRAB OR KOX-1 OR TETR OR EVEN-SKIPPED OR LACR OR E
                S (L22 OR L23) (P) L4
           9870 S L21 (P) L8
               8 S L3 (P) L24 (P) L25
126
L27
               4 DUPLICATE REMOVE L26 (4 DUPLICATES REMOVED)
                S L27 NOT (L7 OR L16)
               2 S LIM MOON/AU
L30
                S EDWARDS CYNTHIA/AU.
             24 S FRY KIRK/AU
                S BRUICE THOMAS/AU
                   STARR DOUGLAS/AU
              0
                S LAURANCE MAGAN/AU
             26
                S KWOK YAN/AU
             68 S L29 OR L30 OR L31 OR L32 OR L33 OR L35
L37
                S L36 AND L1
L38
              0 S L37 NOT L7
=> log y
COST IN U.S. DOLLARS
                                                    SINCE FILE
                                                                    TOTAL
                                                         ENTRY
                                                                  SESSION
FULL ESTIMATED COST
                                                        194.07
                                                                   194.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                                    SINCE FILE
                                                                    TOTAL
                                                         ENTRY
                                                                  SESSION
CA SUBSCRIBER PRICE
                                                         -3.26
                                                                     -3.26
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STN INTERNATIONAL LOGOFF AT 17:11:25 ON 14 SEP 2003

s laurance magan/au